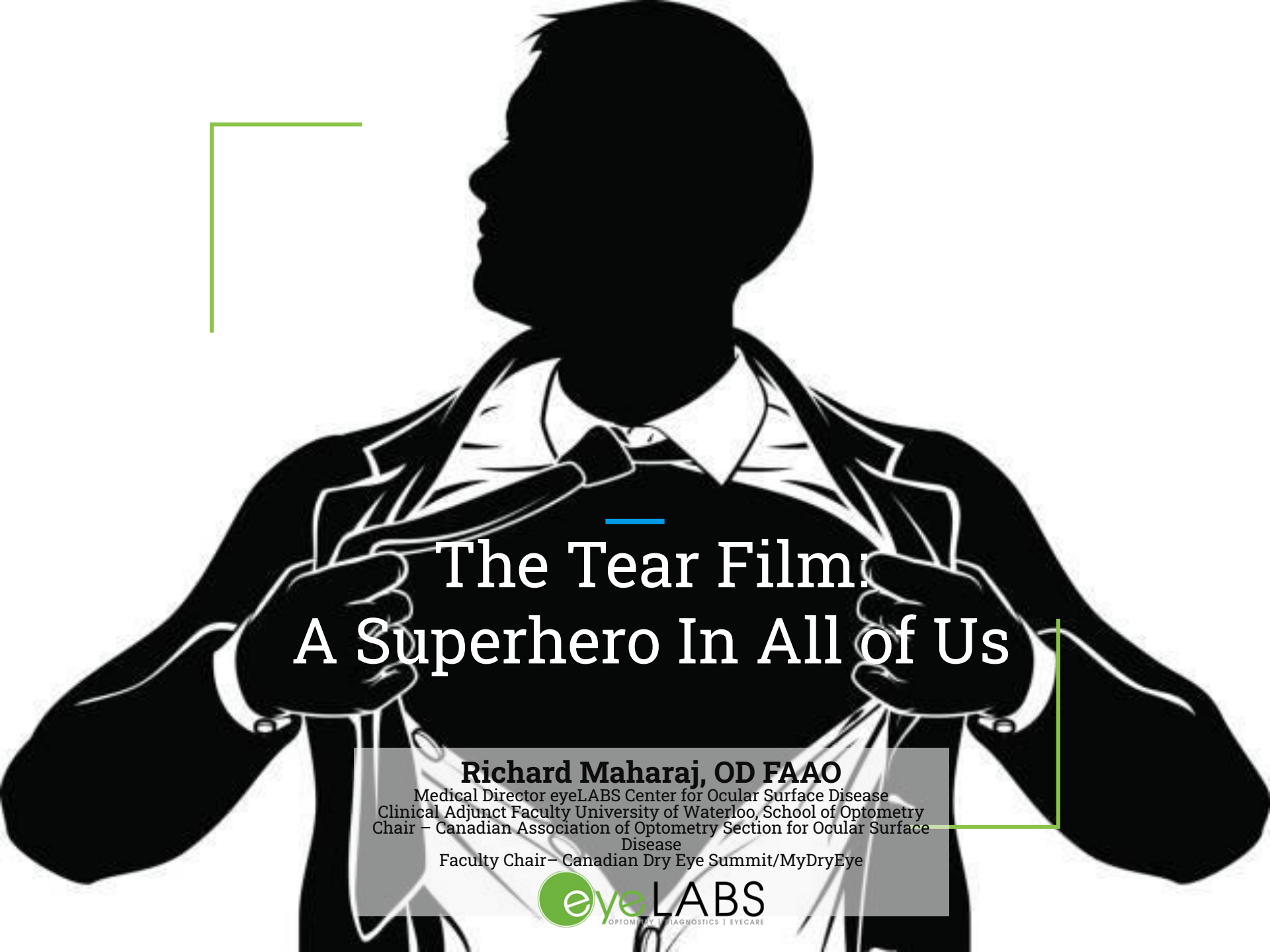

The Tear Film:
A Superhero In All of Us

Richard Maharaj, OD FAAO
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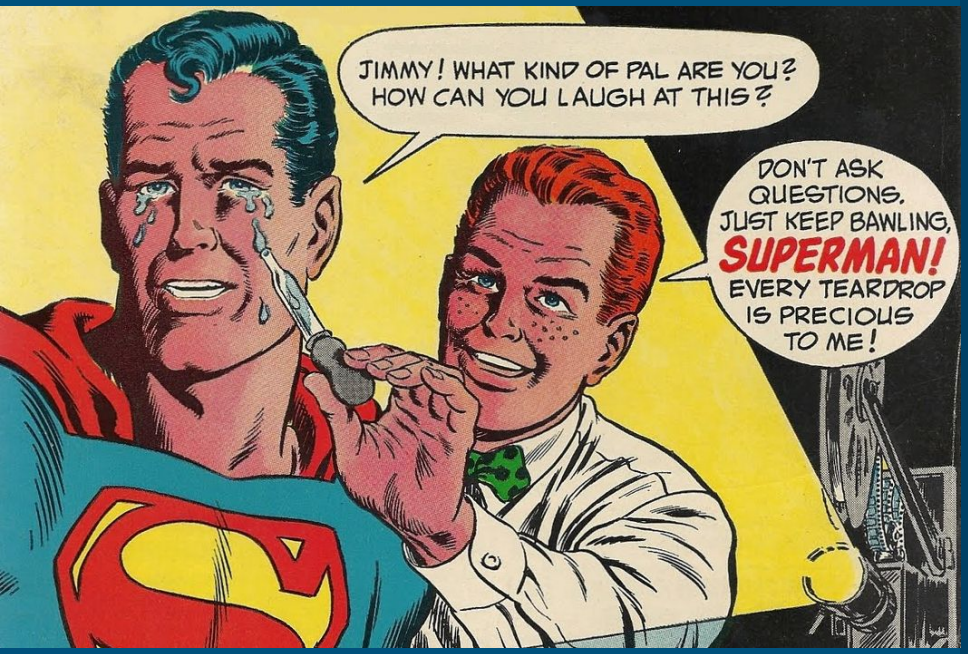
Chair – Canadian Association of Optometry Section for Ocular Surface Disease
Faculty Chair– Canadian Dry Eye Summit/MyDryEye

eyeLABS
OPTOMETRY | DIAGNOSTICS | EYECARE



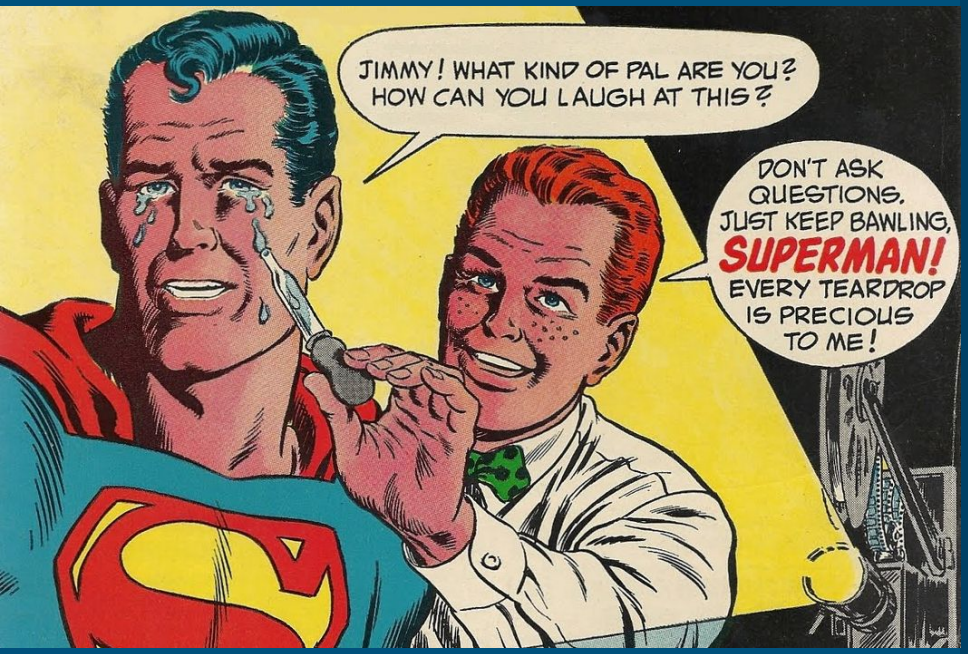
Disclosures

Consultancies with the following industry partners:

- –Labtician-Thea
- –Johnson and Johnson Vision
- –I-MED pharma
- –Allergan
- –Novartis
- –Alcon
- –InMode Aesthetics
- –Sun Pharma Canada

Financial relationship with the following companies

- –MyDryEye Ltd
- - AI4Eyes



Objectives

1. Understanding the current anatomy of the tear film
2. Exploring a DED patient subtypes
3. Applying a practice-based approach to managing DED*

*A complete list of treatment options will not be discussed for each patient subtype

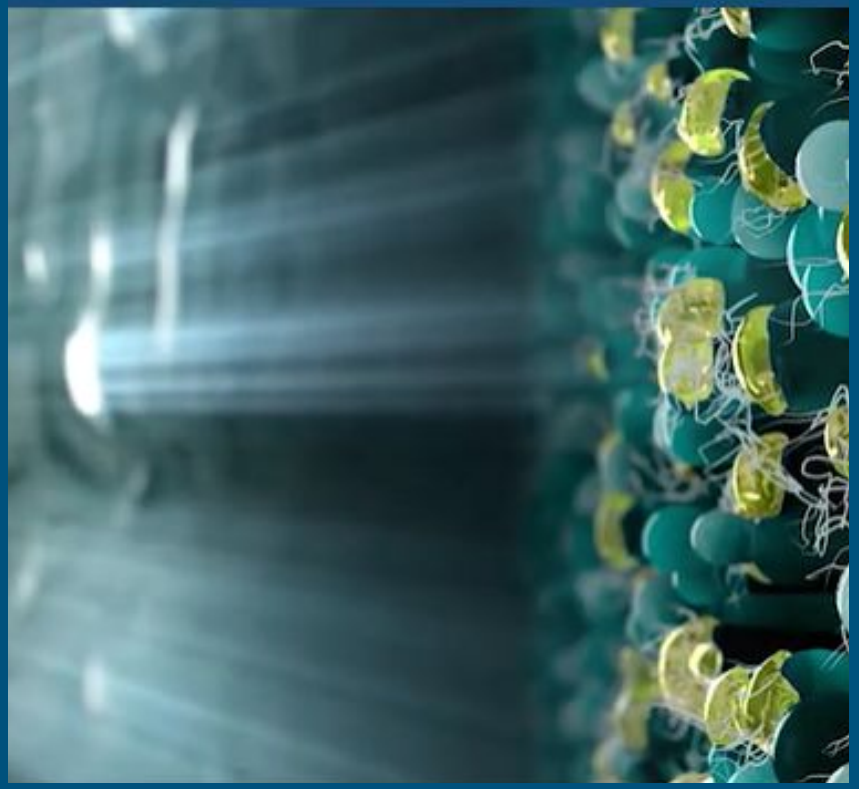
How do you approach DED?

- What is your biggest challenge in the DED space?
- What has been your easiest hurdle to overcome in managing DED?
  - Diagnosing?
  - Treatment plan?
  - Paralleling my DED care to everything else?
  - Others?
- Why do you think DED is not uniformly treated by ECP's?

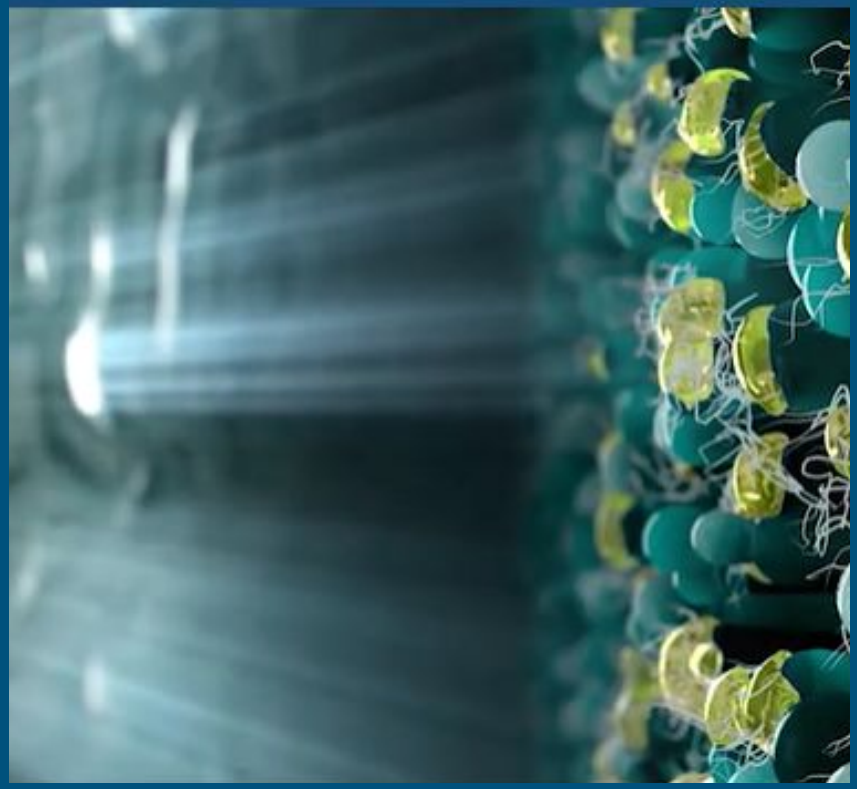
Modern Ocular Surface Anatomy

Tear film anatomy

- **Mucins are produced by goblet cells of the conjunctival and corneal epithelium**
  - form a protective, smoothing layer that acts as an anchor **for the aqueous component**
- **The aqueous component is produced by the lacrimal gland**
  - contains a variety of proteins, including growth factors, antioxidants, and electrolytes
  - When corneal damage occurs, the tear film can help heal the cornea by way of feedback loops that upregulate growth factors and beneficial components in the lacrimal gland
- **Lipids are produced by the meibomian glands and provide a barrier to evaporation from the environment**
  - contains triglycerides, fatty acids, waxes and sterols

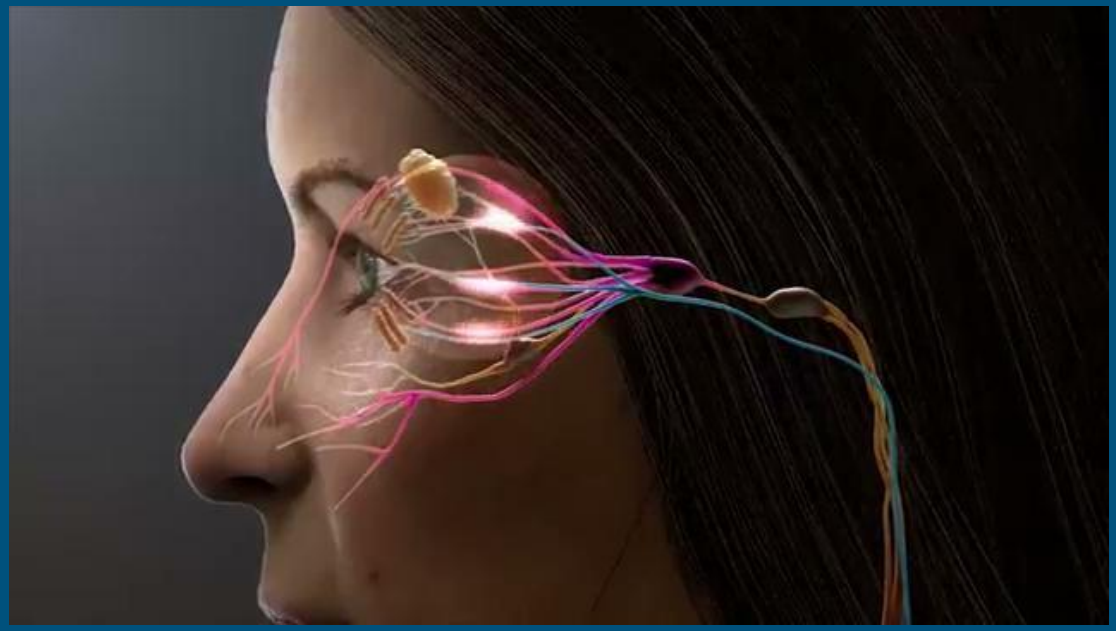


Tear film anatomy



- **>2000 different molecules, including proteins, metabolites, lipids, and mucins**
- **Numerous biologically active growth factors are secreted by the lacrimal gland, including**
  - Nerve growth factor **(NGF)**, which may play a role in ocular surface homeostasis by stimulating epithelial cell proliferation and innervation
  - Epidermal growth factor **(EGF)**, which is a critical regulator in corneal wound healing and may play a role in goblet cell secretion
  - Transforming growth factor beta (TGF-β), which promotes normal growth and differentiation of ocular surface epithelium, suppresses inflammation, and may also play a role in immune regulation

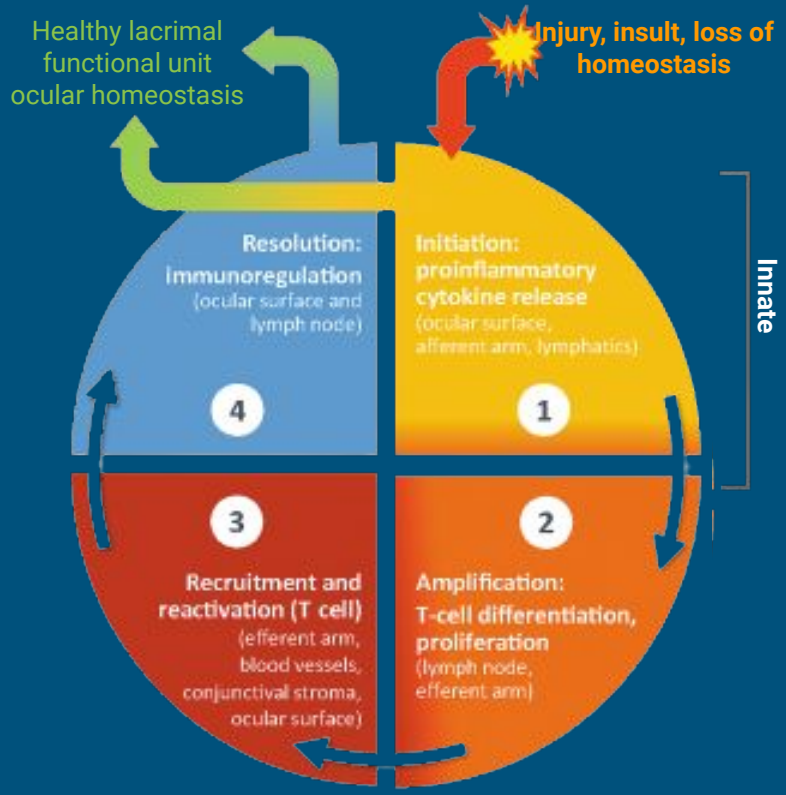
The lacrimal functional unit (LFU)



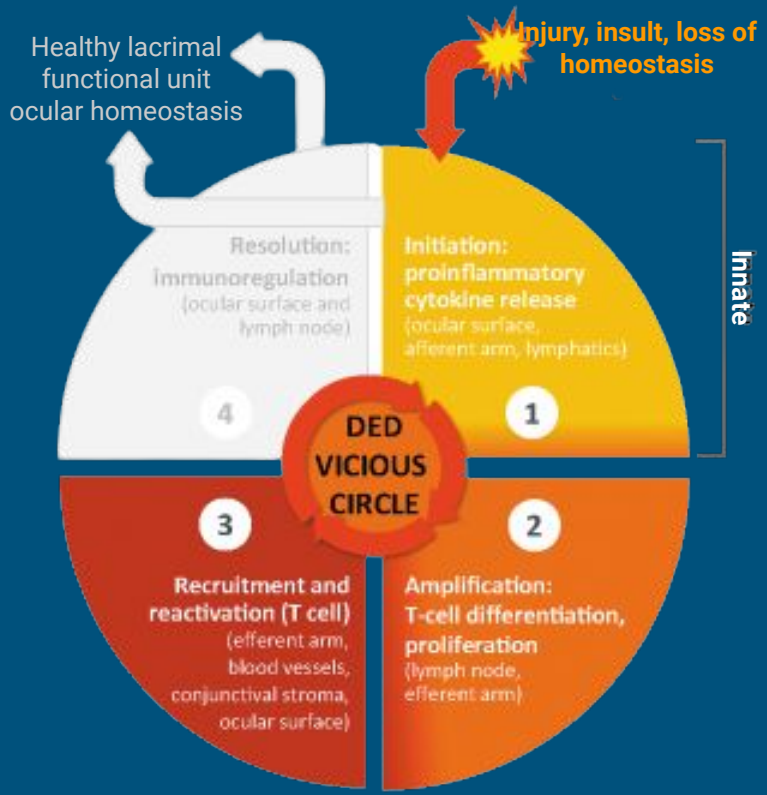
- Ocular surface homeostasis is mainly regulated by the trigeminal parasympathetic pathway
  - stimulation of corneal sensory and conjunctival nerves
  - afferent signals to the trigeminal parasympathetic reflex to maintain tear film homeostasis
- The sympathetic pathways can modulate tear flow and composition
- Stimulation through the nasal cavity contributes to ⅓ of basal tearing

The Tear film Immunological response

Normal Ocular Immune response:
Regulated adaptive



Pathological ocular immune response: **Dysregulated adaptive**



Laura M. Periman, Victor L. Perez, Daniel R. Saban, Meng C. Lin, and Piergiorgio Neri.Journal of Ocular Pharmacology and Therapeutics.Apr 2020.137-146

DED Patient Subtypes

DED Patient Subtypes

Episodic - Signs and symptoms are periodic and transient. Tend to be exacerbated by environment, lifestyle, evaporative triggers (CLs, digital use, etc.

Chronic -Signs and symptoms are more consistent and underpinned by chronic inflammation. Those that are not “episodic” are by thus “chronic.”

Recalcitrant - Chronic patients with a suboptimal response to chronic treatment. Often symptoms can be disproportionate to signs.

P. Karpecki, C. Prokopich, L. Racine, E. Bitton, B. Caffery, P. Harasymowycz, L. Michaud, V. Pegado, J.-S. Dufour, P. Neumann, A. Webber and J. Ashkenas, "Dry Eye Diseases and Ocular Surgery: Practical Guidelines for Canadian Eye Care Practitioners," *Canadian Journal of Optometry,* vol. 79, no. 4, pp. 19-33, 2014.

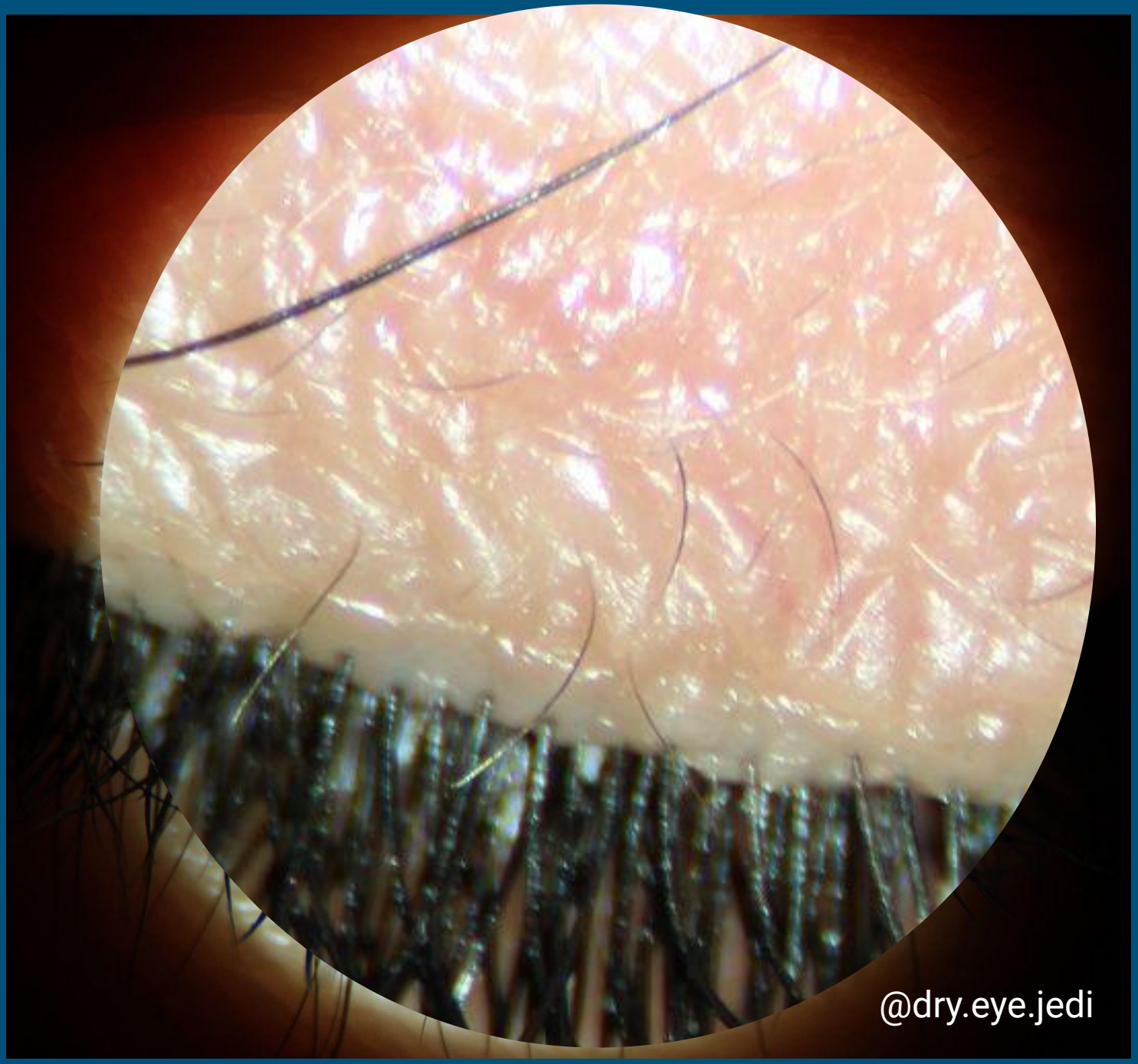
The Episodic patient

Presentation

- Likely <24 y.o. demographic, +/- CL wearer
- Symptoms mild (DEQ 6-11, SPEED 4-7)
- Signs
  - trace corneal or conjunctival staining
  - TBUT suboptimal at presentation
  - Meibography minimal morphological indications of MGD
  - Osmolarity ~300 (highly variable)
- presents during lifestyle intense, environmentally volatile times of year
- “It must be because of….”

Clinical Pearls

1. **Examine eyelash roots for cylindrical dandruff**
2. **Evert lids and look for Lid Wiper Epitheliopathy (LWE)**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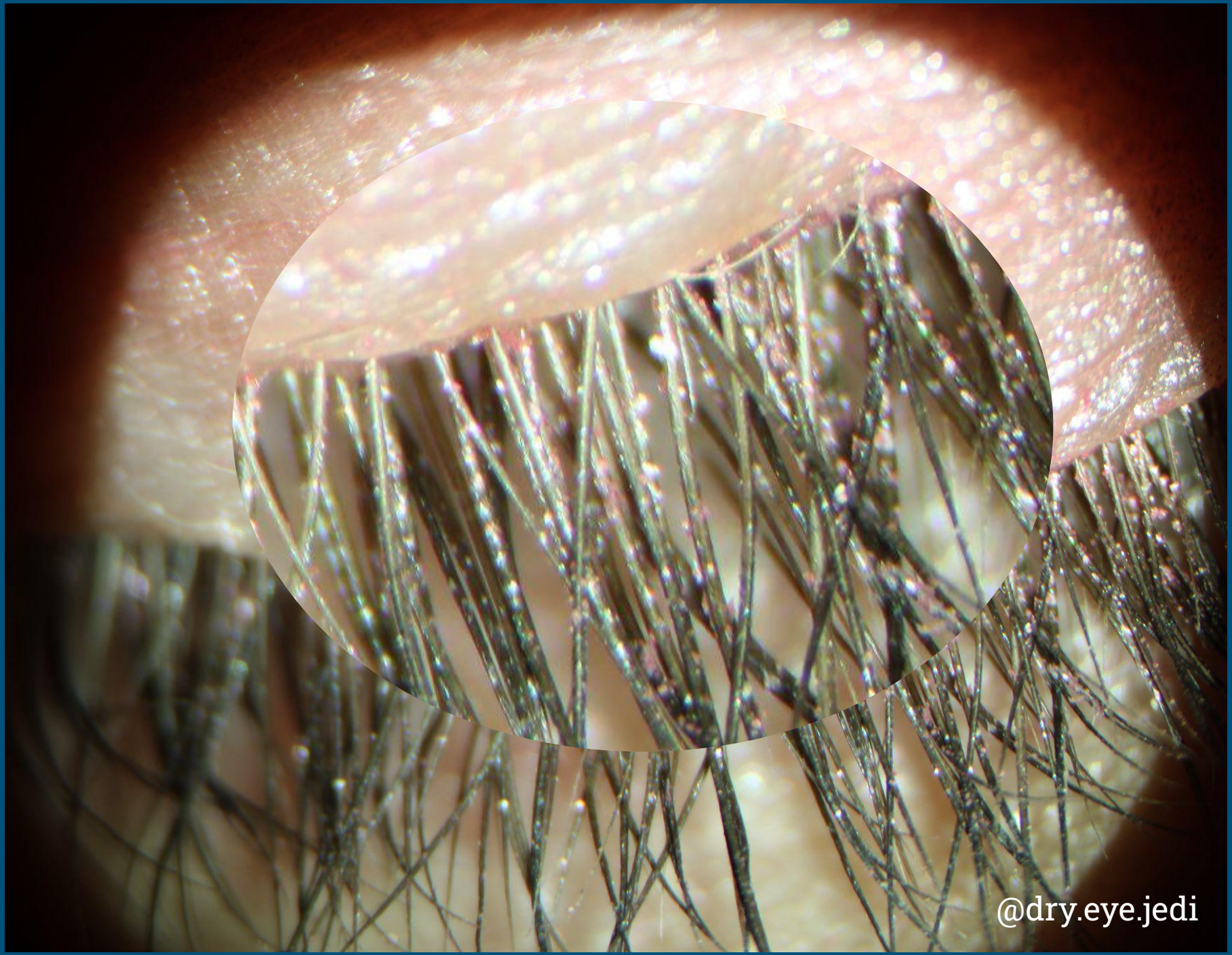
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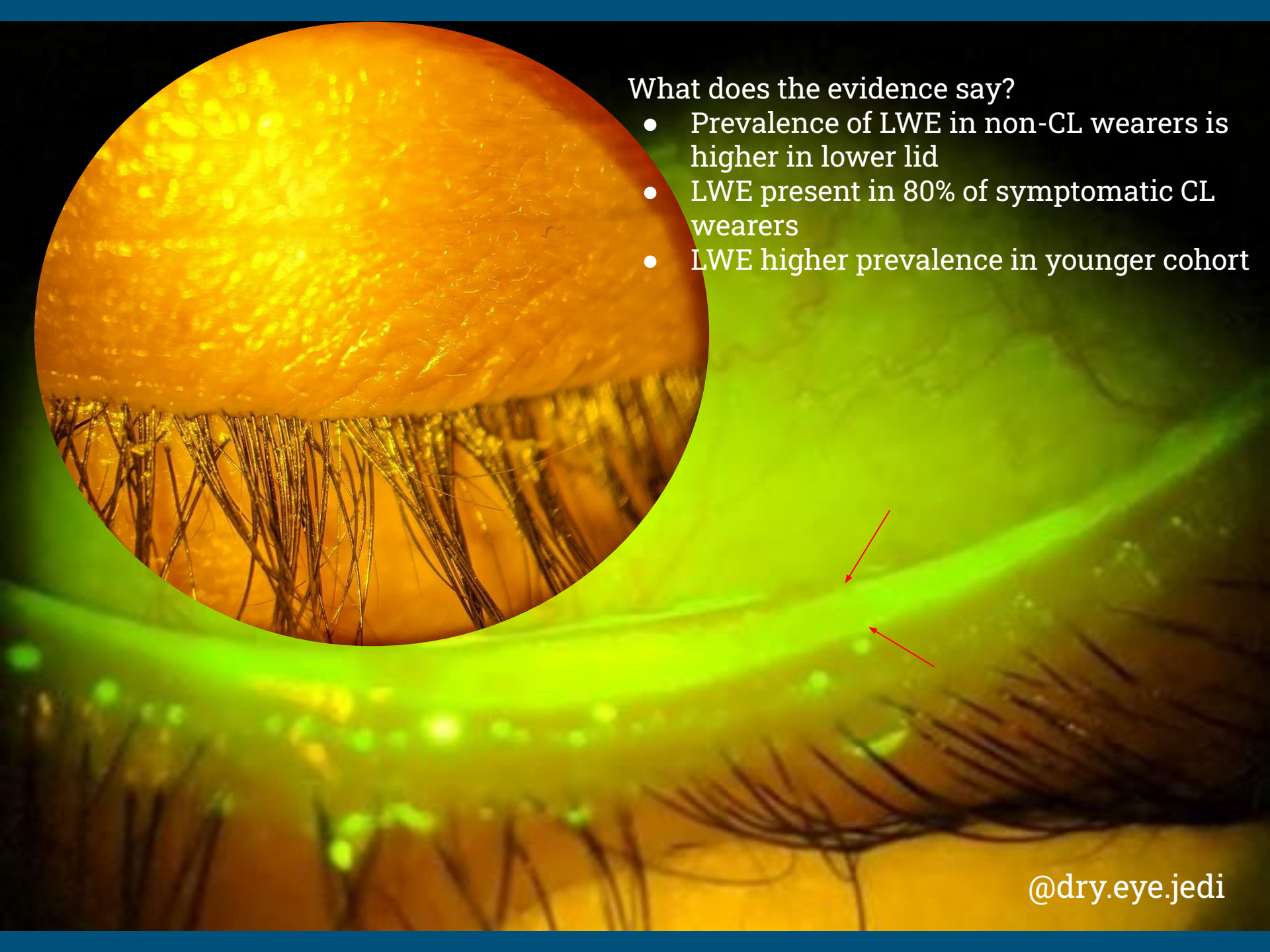

What does the evidence say?

- Prevalence of LWE in non-CL wearers is higher in lower lid
- LWE present in 80% of symptomatic CL wearers
- LWE higher prevalence in younger cohort

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The Episodic patient

- Counsel on lifestyle modifications
- Triage against dry eye contributors (allergy, autoimmune diseases, contact lens, eye surgery)
- digital device use
- Medications (eg, antidepressants, antihistamines, diuretics, glaucoma drops, hormone replacement therapy
- Anxiety and depression
- Supportive eyelid hygiene, omega 3s, warm compresses

Treatments

- Hyaluronate based non-preserved lubricants
  - target friction reduction
  - support dynamics of blink
- TTO based cleansers
  - Anti-bacterial
  - Anti-demodectic
- Loteprednol etabonate (0.25% or 0.5% depending on severity
  - mild 1 gt 0.25% bid x 2/52
  - moderate 1 gt 0.5% bid x 2/52

Treatment Pearls:

1. **Focus on prevention - reduce evaporative triggers (digital screen use, cosmetic offenders, recognize flare ups)**

How to choose the right drop?

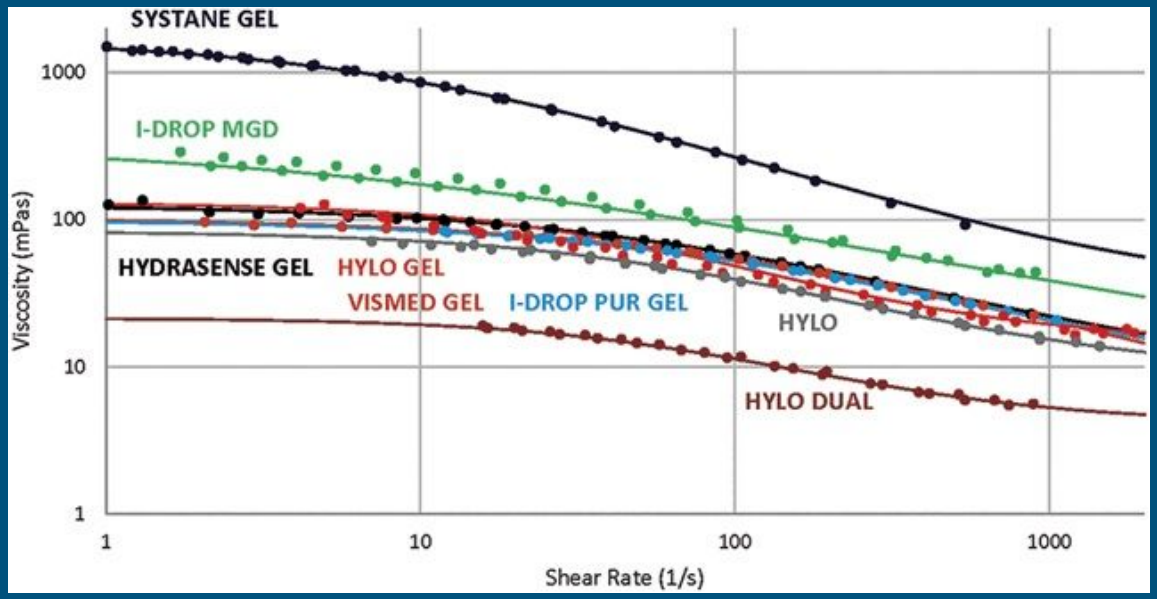

Figure 1.

Shear-thinning behavior—group A. All artificial tears included in group A clearly demonstrated low and high shear Newtonian plateaus separated by a zone of significant shear thinning, but some exhibited higher overall viscosity than others.

- Optimal shear thinning properties with blink acceleration and high residence time and clarity at blink intervals for clear vision
- High viscosity when eye open
- Low viscosity when blinking (friction avoiding)
- Visual blur occurs above 30 mPas of viscosity

Arshinoff SA, Hofmann I, Nae H. The role of rheology in tears and artificial tears. J Cataract Refract Surg 2021;47:655–661

How to choose the right drop?

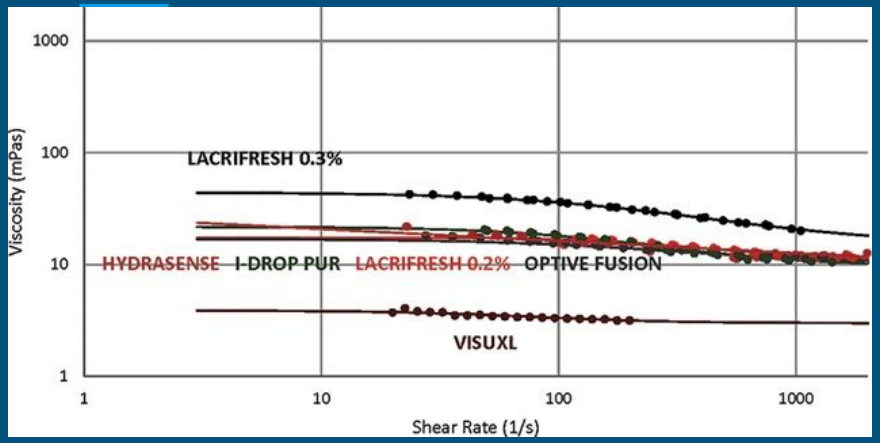

Figure 2.

Shear-thinning behavior—group B. Group B artificial tears demonstrated rheological behavior similar to those in group A (Figure 1), but the rheological curves exhibited lower initial viscosity and moderate shear-thinning behavior.

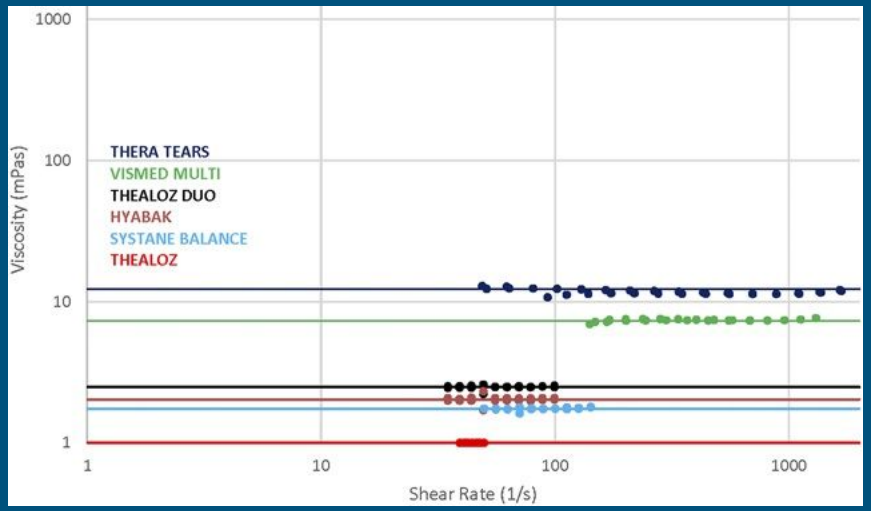

Figure 3.

Newtonian behavior—group C. All members of group C demonstrated no change in viscosity with increasing shear rate and therefore illustrate typical Newtonian behavior.

Arshinoff SA, Hofmann I, Nae H. The role of rheology in tears and artificial tears. J Cataract Refract Surg 2021;47:655–661

The Chronic patient

Presentation

- Likely 45-64 y.o. demographic, +/- CL wearer, female>male,
- Symptoms mild-moderate (DEQ >12, SPEED 7-10)
- Signs
  - inferior corneal, n/t conjunctival staining, +/- SLK or perilimbal staining
  - TBUT <5s
  - Meibography -terminal ductule distention, truncation and periductal fibrosis
  - Osmo >306 (highly variable)/+ve MMP-9

Clinical Pearls

1. **Careful attention to superior bulbar conjunctiva**
2. **Diagnostic MG expression is a MUST (cotton-tip or MGE, avoid finger)**


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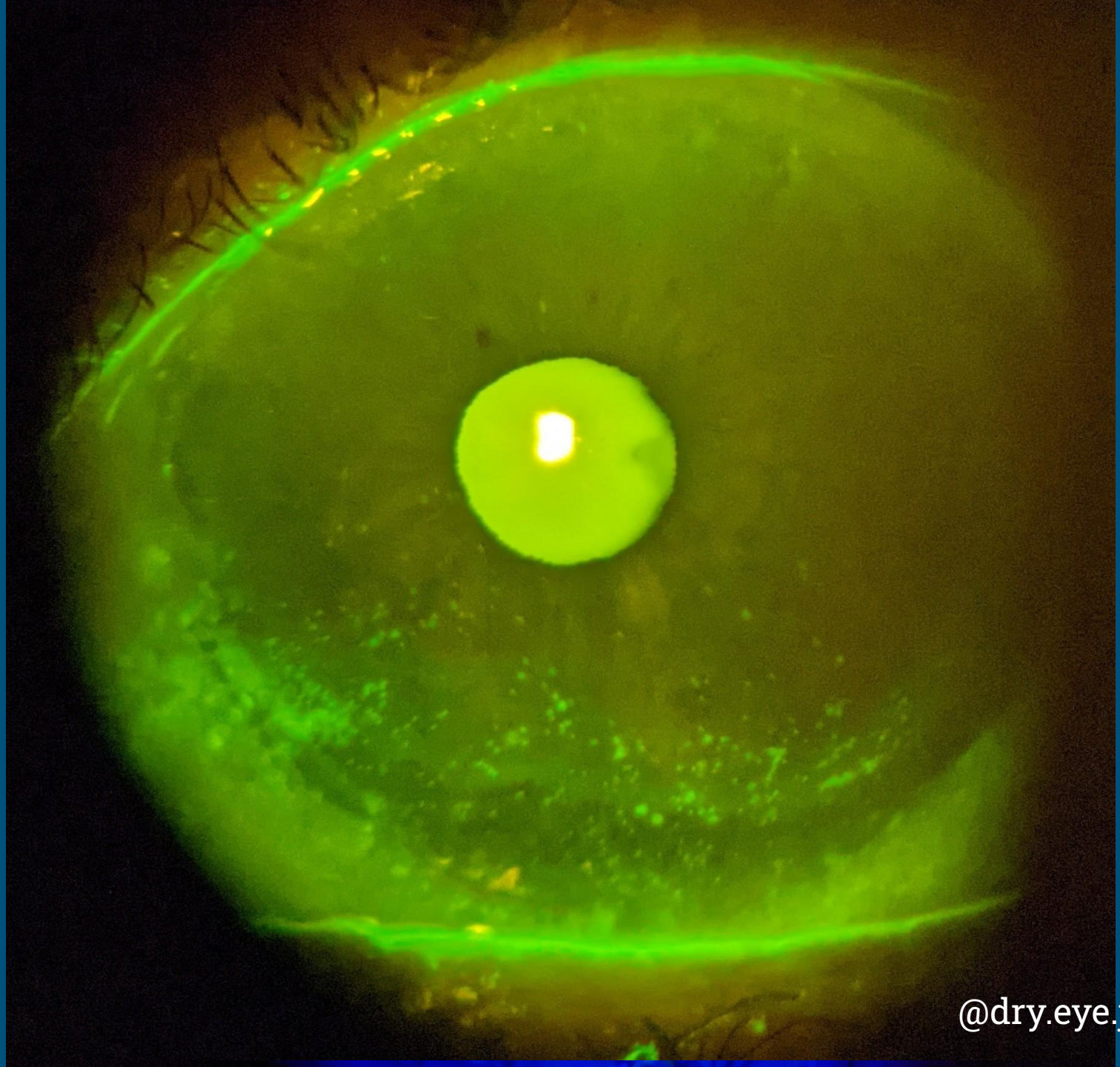
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What does the evidence say?

- MGD is a component in up to 86% of DED patients
- Functional MG expression under high mag to fully diagnose MGD
- Myth: MGD = toothpaste expressibility

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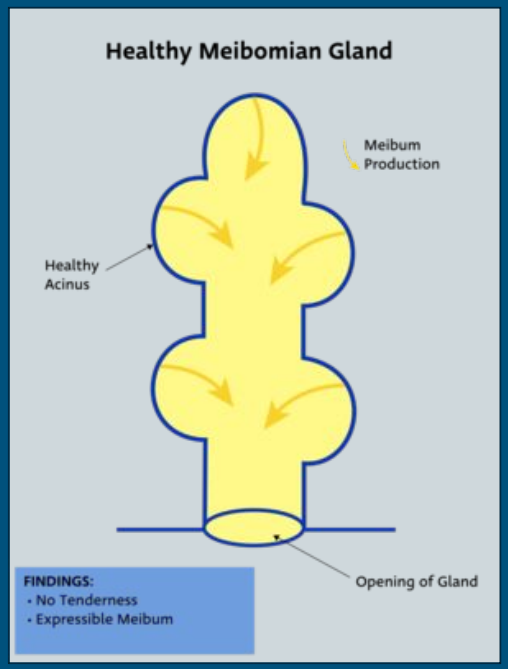
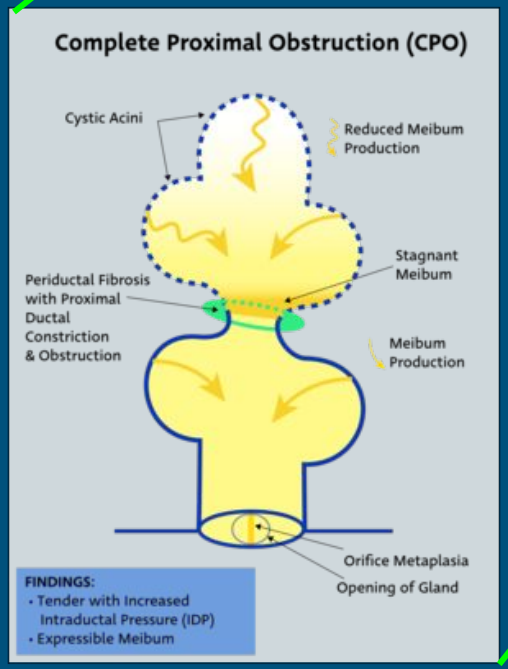
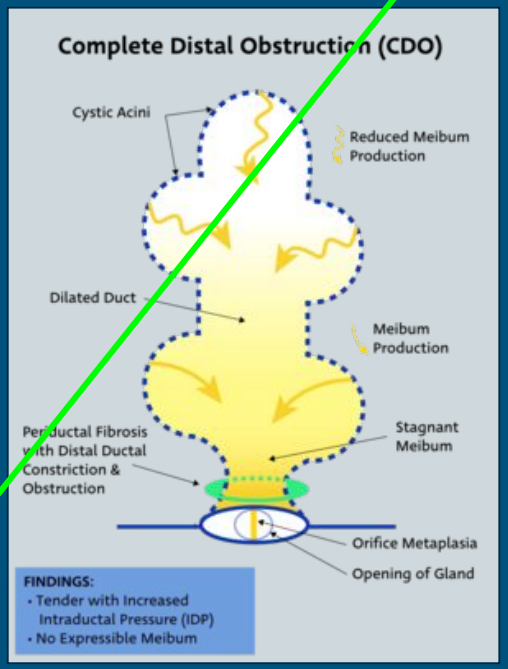

Healthy Meibomian Gland
Meibum Production
Healthy Acinus
Opening of Gland
FINDINGS:
• No Tenderness
• Expressible Meibum


Complete Proximal Obstruction (CPO)
Cystic Acini
Reduced Meibum Production
Stagnant Meibum
Periductal Fibrosis with Proximal Ductal Constriction & Obstruction
Meibum Production
Orifice Metaplasia
Opening of Gland
FINDINGS:
• Tender with Increased Intraductal Pressure (IDP)
• Expressible Meibum


Complete Distal Obstruction (CDO)
Cystic Acini
Reduced Meibum Production
Dilated Duct
Meibum Production
Stagnant Meibum
Orifice Metaplasia
Opening of Gland
FINDINGS:
• Tender with Increased Intraductal Pressure (IDP)
• No Expressible Meibum

The Chronic patient

- Include episodic treatment options
- Immunomodulation options (cyclosporine A, lifitegrast)
- In-office thermal gland expression where applicable, i.e. LipiFlow, iLux, Radio Frequency (skin type)
- Manage underlying contributors (SS, RA, Thyroid, etc.)

Treatments

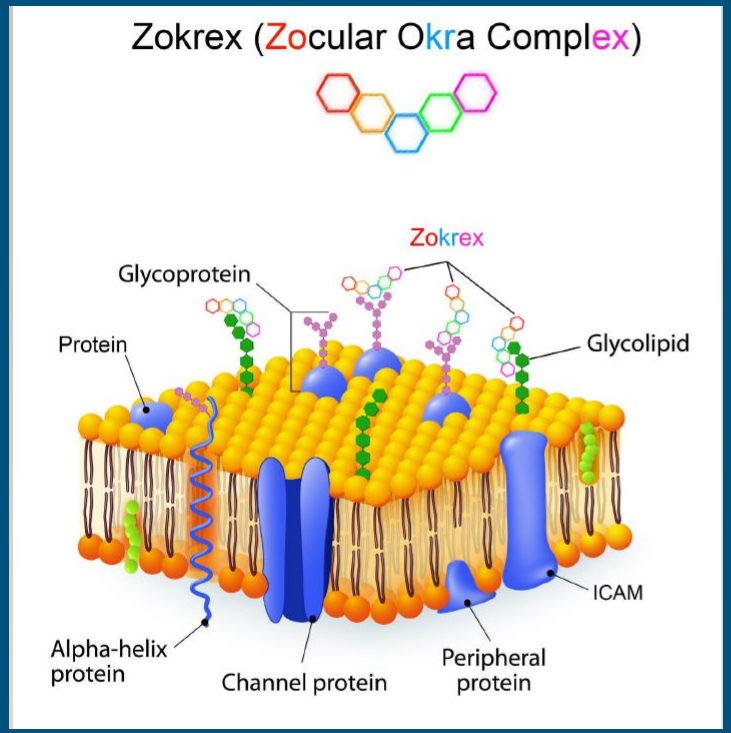
- In-office eyelid hygiene (q 6/12)
  - Zocular® Eyelid System Treatment (ZEST)
    - anti-demodectic, anti-inflammation, analgesic)
  - Microblepharoexfoliation (A/B Max, BlephEx)
- Intense Pulsed Light
  - Anti-inflammatory via photo-thrombolytic effect
  - Anti-demodectic/bacterial
  - Photobiomodulation
  - Initial 4 treatments, with q6-12/12 maintenance

Treatment Pearls:

1. **Interventional eyelid management**
2. **Multimodal approach**

Zocular® Eyelid System Treatment

- ZocuShield - extract of *Abelmoschus esculentus* (okra)
- Polysaccharide that exerts anti-demodectic, antibacterial and anti-inflammatory effect
- Polysaccharides can modulate cell membrane to dynamically
- Rather then completely blocking 1 pathway, it can modulate multiple channels to optimize and counterbalance inflammatory activity

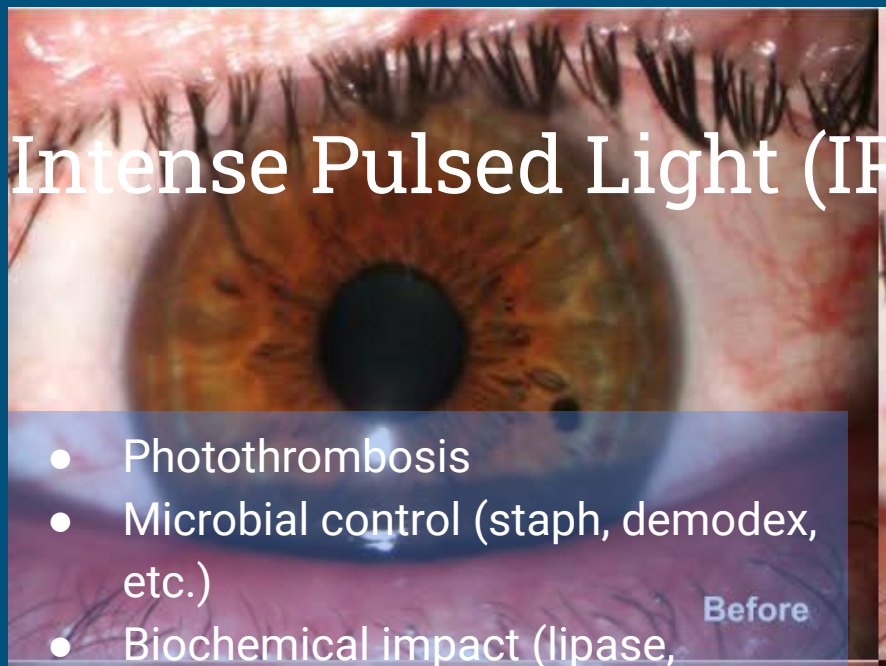


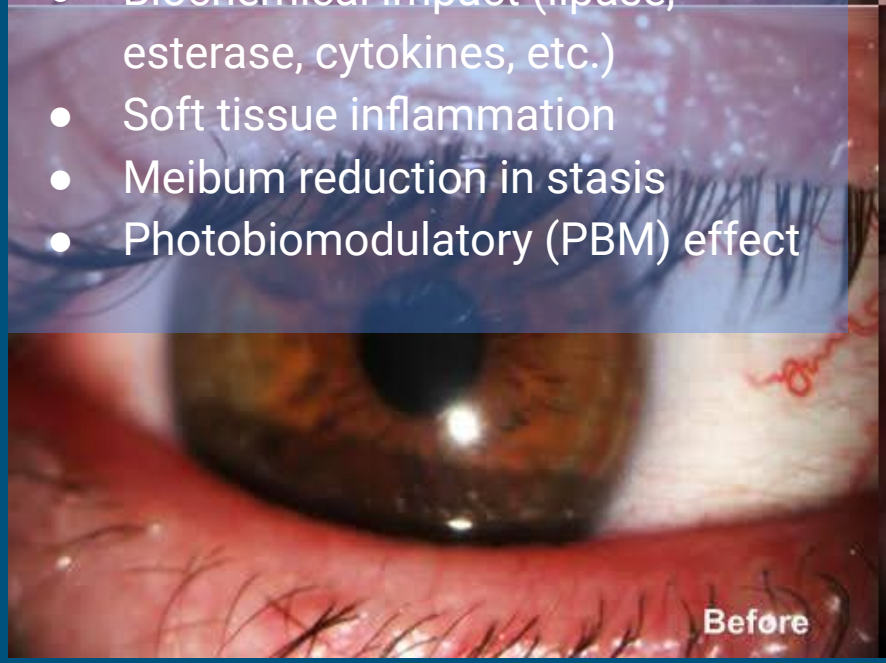
S. Narayanan, N. Kasraie, M. Stewart and e. al., "Lid margin debridement improves contact lens discomfort caused by meibomian gland dysfunction.," Invest Ophthalmol Vis Sci, vol. 60, no. 9, p. 6368, 2019.

L. Wenting and L. Gong, "Anti-demodectic effects of okra eyelid patch in Demodex blepharitis compared with tea tree oil," Exp Ther Med, vol. 21, no. 4, p. 338, 2021.

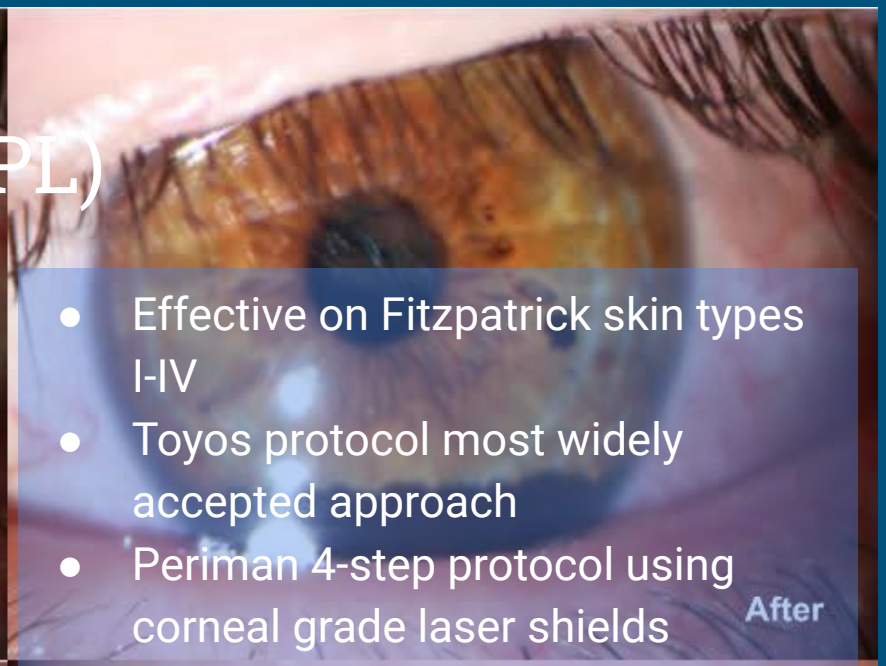
Intense Pulsed Light (IPL)

- Photothrombosis
- Microbial control (staph, demodex, etc.)
- Biochemical impact (lipase, esterase, cytokines, etc.)
- Soft tissue inflammation
- Meibum reduction in stasis
- Photobiomodulatory (PBM) effect





- Effective on Fitzpatrick skin types I-IV
- Toyos protocol most widely accepted approach
- Periman 4-step protocol using corneal grade laser shields
- Maharaj modified 3-step with corneal grade laser shields
- Multimodal with Radio Frequency, LLLT, thermal expression (LipiFlow, iLux, etc.)
- Training and dermatology background



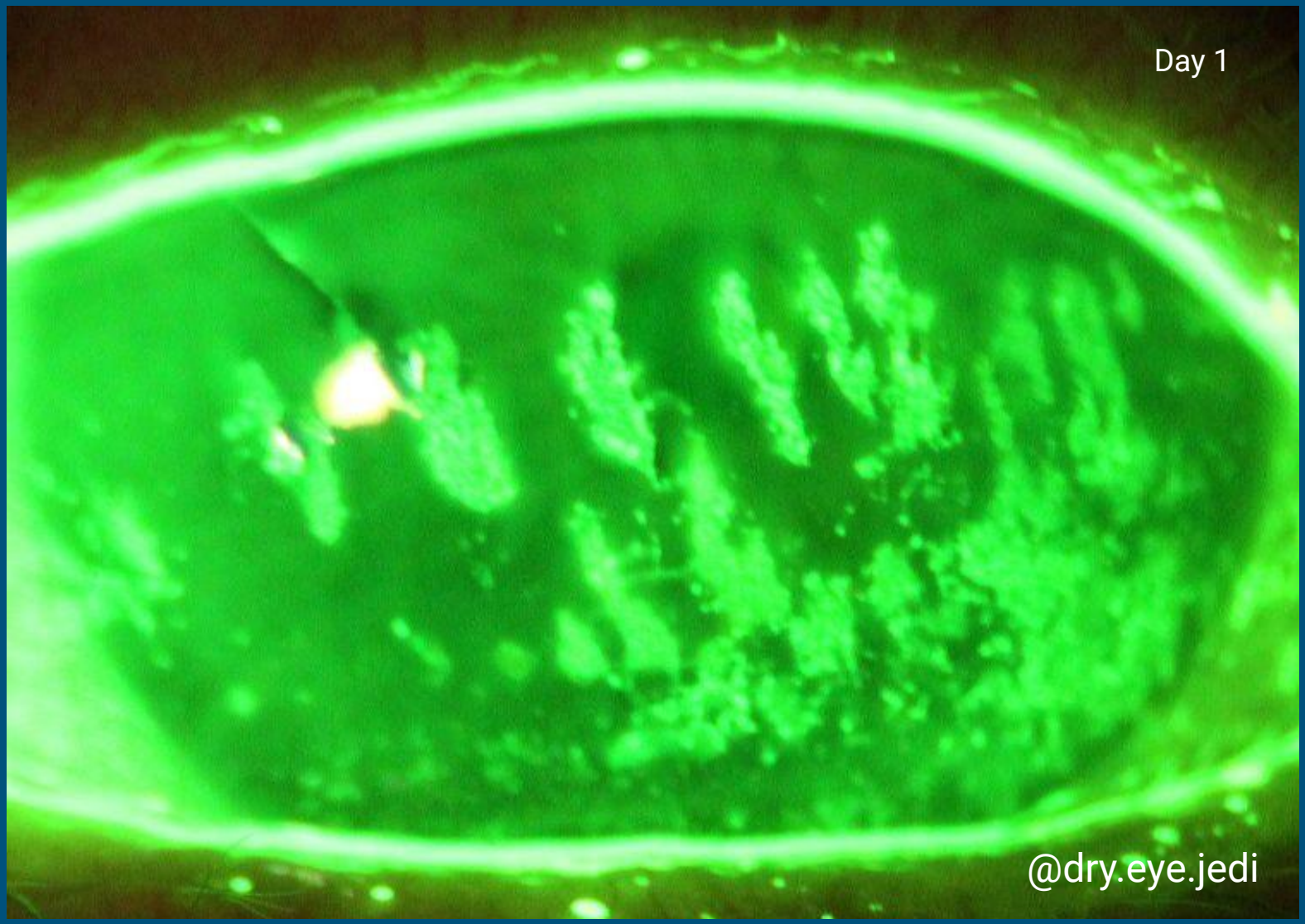
The Recalcitrant patient

Presentation

- Likely 65+ y.o. demographic, systemic contributors (SS, RA, History of eye surgery, medicamentosa), female>male,
- Symptoms moderate-severe (DEQ >12, SPEED 11+)
- Signs
  - filamentary keratitis global corneal staining, conjunctival staining, TBUT instant, poor MG expressibility
  - Meibography - advanced truncation
  - Osmo >306 (highly variable)/+ve MMP-9
  - Symptoms>>signs (neuropathy) v. signs>>>symptoms (neurotrophic)

Clinical Pearls

1. **While signs can be severe, pay attention to mental health of the patient**
2. **History is the most important data point!**


Day 1
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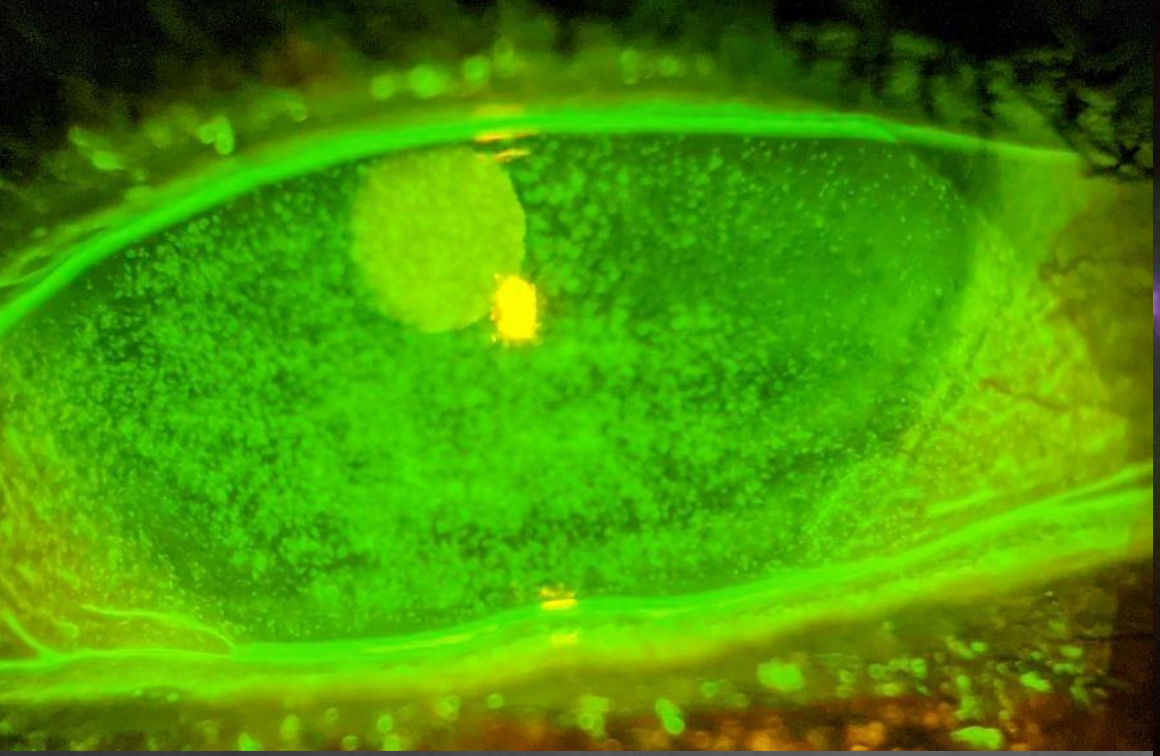

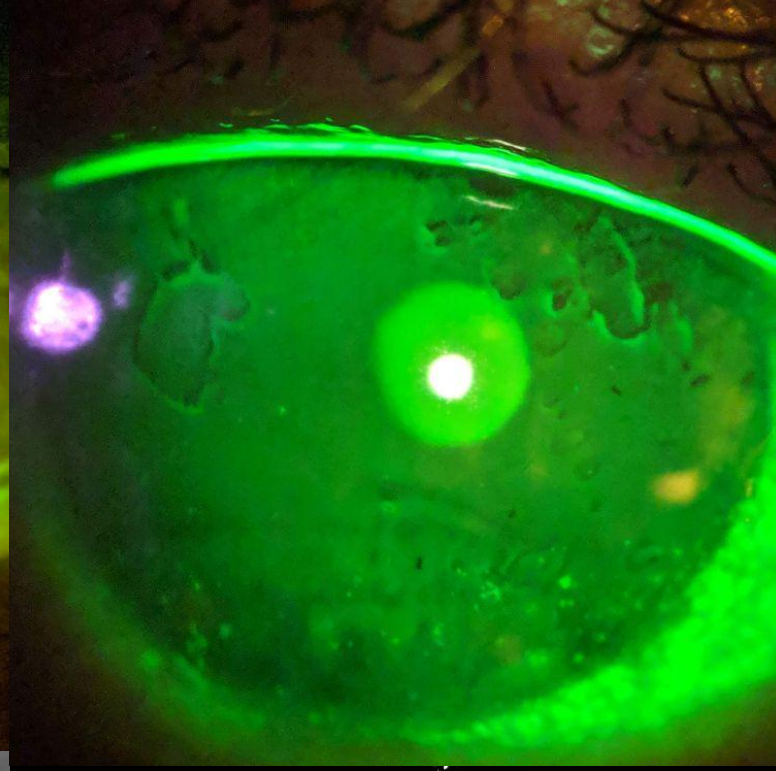

What does the evidence say?

- Chronic untreated DED will impact corneal nociceptive integrity invariably contributing to a wider gap between signs and symptoms
- Anxiety, depression, mood disorders, neuroticism may be associated with symptom exacerbation

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The Recalcitrant patient

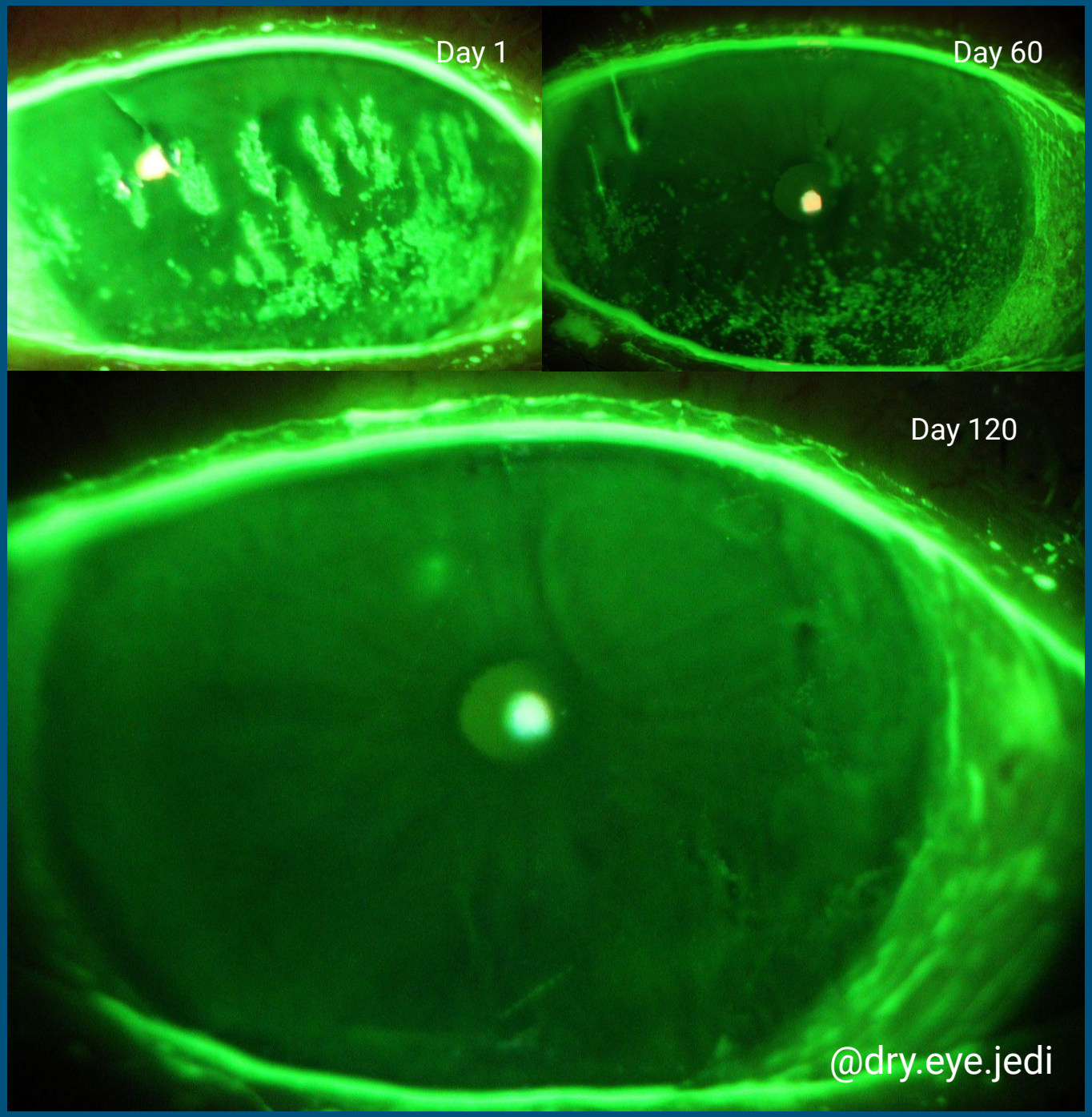
- Include chronic treatment options
- Mental health support/referral
- Manage underlying contributors (SS, RA, Thyroid, etc.)
- Amniotic membranes (cryopreserved and dehydrated options)
- scleral contact lenses

Treatments

- Autologous Serum Eye Drops (Post-clotted blood)
  - Rich in epidermal, fibroblast and nerve growth factors (EGF, FGF, NGF)
  - Increases epithelial proliferation and healing as well as decrease inflammation
  - transforming growth factor-beta (TGF-β) which can decrease stromal transparency, so concentrations are often kept at 20%
- Platelet Rich Plasma
  - transforming growth factor-beta (TGF-β) which can decrease stromal transparency
  - Higher concentration of GFs and reduced serum cytokines
  - Evidence to support increasing sub-basal nerve plexus density

Treatment Pearls:

1. **Set appropriate expectations**
2. **Pain management considerations**


Day 1
Day 60
Day 120
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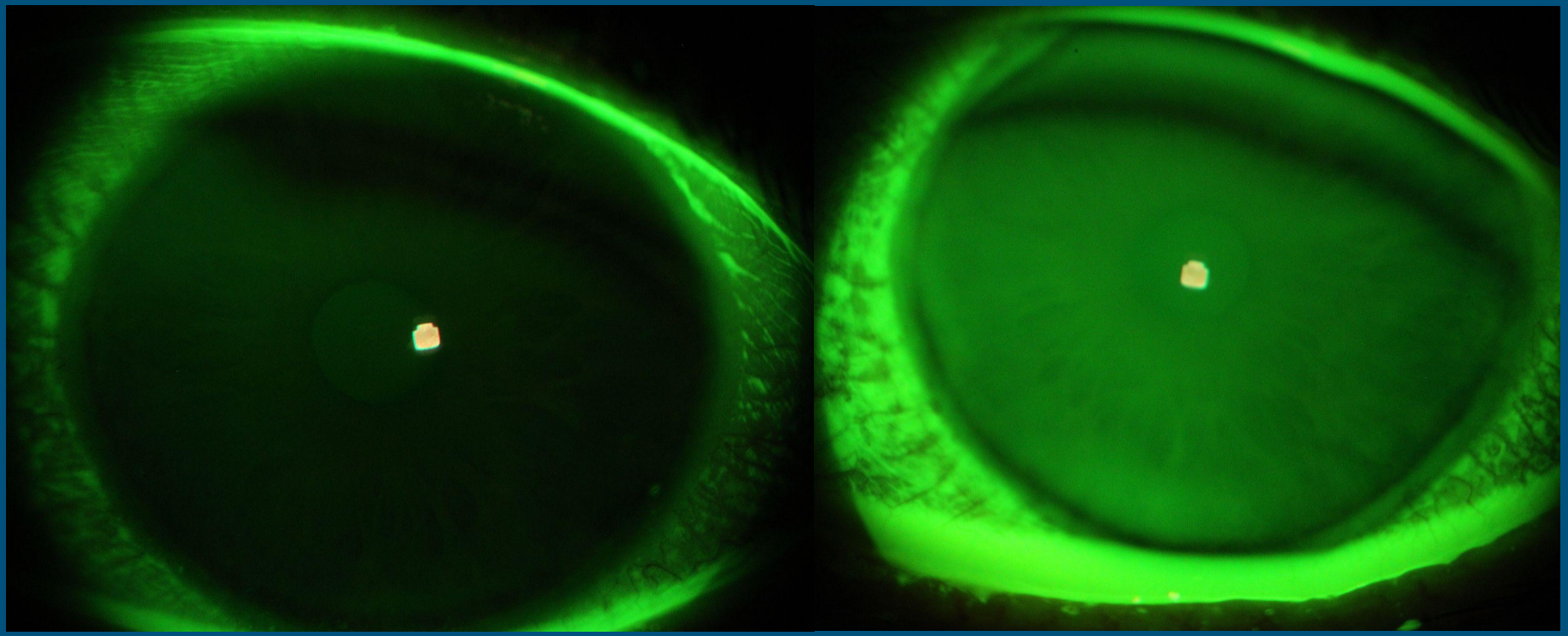
Neuropathic Pain



What does the evidence say?

- Transient receptor potential melastatin 8 (TRPM8) cold thermoreceptors may be able to modulate evaporative triggers of pain
- Objective pain measurement is limited
- Myth: Neuropathic pain is always 10/10 level

DED Patient Subtypes

Episodic - Signs and symptoms are periodic and transient. Tend to be exacerbated by environment, lifestyle, evaporative triggers (CLs, digital use, etc.

Chronic -Signs and symptoms are more consistent and underpinned by chronic inflammation. Those that are not “episodic” are by thus “chronic.”

Recalcitrant - Chronic patients with a suboptimal response to chronic treatment. Often symptoms can be disproportionate to signs.

P. Karpecki, C. Prokopich, L. Racine, E. Bitton, B. Caffery, P. Harasymowycz, L. Michaud, V. Pegado, J.-S. Dufour, P. Neumann, A. Webber and J. Ashkenas, "Dry Eye Diseases and Ocular Surgery: Practical Guidelines for Canadian Eye Care Practitioners," *Canadian Journal of Optometry,* vol. 79, no. 4, pp. 19-33, 2014.

Conclusion

- Episodic and Chronic make up 80% of the DED patients in practice
- A modern interventional approach rather than a dated reactive one reflects the current level of understanding of the disease
- By definition DED is multifactorial which is reflected in the growing number of modes of therapy
- The silver bullet to preventing and managing DED is…


Thank you
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